"Characterization of Mucus and Mucin in Bronchoalveolar Lavage Fluids from Infants with Cystic Fibrosis"
by
University of North Carolina at Chapel Hill,
Dr. Terry Noah

Prior to my report on the proposed study by Dr. Noah, I would like to provide a little background information. First, I am a parent with an 18-year-old son who has Cystic Fibrosis (CF). He presented meconium ileus at birth and emergency surgery was performed 24 hours later. After numerous tests, he was pronounced "normal" and we were told to go on with our lives. I did not feel comfortable with that diagnosis, and so pursued the issue. Finally, at 3 months of age, he was given the sweat test using the pylocarpine, not the electrodes, and he tested positive for CF. We have continued to visit the CF Centers regularly every 3 months, or more often as needed, for the last 18 years. He has been hospitalized 3 times for pulmonary exacerbations, and has participated in one study already. We have used some of the cutting edge antibiotic treatments and therapies even though there have been no clinical studies done to prove their effectiveness. Basically, I feel that any extra time I can buy my son is worth the risk; if the risk is minimal. Daily life with a child is a constant risk, especially a child with CF. I am my son's advocate. I fight every day to insure that all treat him equally, fairly, and respectfully. This is a difficult battle and one that will never be won until the disease is cured or under control.

I have reviewed the research protocol by Dr. Noah Terry, the consent form and the other documents and information provided. I also bring into the process, my own personal experiences and knowledge of CF and children. Dealing with children is tough; dealing with research on children is even tougher. Fortunately, the government provides strict regulations that must be followed. I feel that this protocol can be approved under two Federal Regulations, 45 CFR 46.406 and 45 CFR 46.407.

*I do NOT consider the protocol to be approvable under 45 CFR 46.404, "No greater than minimal risk". Dr. Noah has documented the risks for 2171 bronchoscopy procedures performed at UNC. The incidence for complication was less than 1%, but that is still a risk for a normal, healthy child. For that reason, this protocol cannot be approved under 45 CFR 46.404.

*I do NOT consider the protocol to be approvable under 45 CFR 46.405, "Greater than minimal risk, but presents the prospect of direct benefit to the individual subjects". The bronchoscopy procedure is greater than minimal risk, so one must evaluate the possibility of direct benefit to the child. At this point, there is no definitive direct benefit. There is the possibility of finding more information that may lead to better therapies and treatments in the future, but there is no direct benefit from this procedure.

*I DO consider the protocol to be approvable under 45 CFR 46.406, "Greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition". As previously stated, there is definitely a risk involved with the bronchoscopy, less than 1%, and there appears to be no direct benefit to the individual at this time. However, the data and information gathered will definitely yield new information about the lungs and their fluids in young CF patients. Perhaps this will yield information about the disease that will lead to better treatments and therapies. In any case, there will be knowledge that is previously unavailable on this disorder and condition and is unable to be obtained in any other way.

*I DO consider the protocol to be approvable under 45 CFR 46.407, "Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children". If one concludes that the risk of bronchoscopy is too great for a child, and so disapproves 45 CFR 46.406, than this protocol will definitely fit here. This research will provide data and information that will help lead to a better understanding of CF lungs and their fluids. CF is a serious problem for those with the disease and their families. It places great strains, both financially and emotionally on all who are involved. There is only one way to solve the problem, and that is by aggressive research which will hopefully lead to a cure or at least a treatment that will allow a CF child to lead a full and "normal" life.

Finally, the research satisfied the conditions of 45 CFR 46.406 and 45 CFR 46.407 and the following conditions are met:

1. "The research presents a reasonable opportunity to further the understanding, prevention or alleviation of a serious problem affecting the health or welfare of children". This protocol

definitely presents an opportunity to further understand the disease, Cystic Fibrosis. Currently, there is no such data available on the young lungs and their fluids.

2. "The research will be conducted in accordance with sound ethical principles". The protocol appears to be very well written, and I can find no major flaws. I do feel that some additions/changes should be made before approval is granted. Whether these changes fall in this category or category 3, I am not sure, but they are definitely needed. There should be a definite amount of drug(s) specified, the level of sedation achieved, and what specific drug(s) will be used. I also feel that there should be a definite set of guidelines about when the procedure will be stopped…what conditions will cause the doctor to stop the procedure? Will the anesthesiologist be present in the OR, or will it simply be the Broncho Team? Who specifically makes up the Broncho Team and who will perform the procedure? This information should be included in the information/consent form. Finally, my biggest complaint is the phrase, "If such complications arise, the researchers will assist you in obtaining appropriate medical treatment, but any costs associated with the treatment will be **billed to you and/or your insurance company**". This is morally and ethically wrong. The child is participating unwillingly in your study, although the parents have granted their permission. If there is a temporary or lasting complication, it should definitely be **treated free of charge** to the parents/child. There is Workman's Compensation for those people injured on the job, there are VA Benefits for injuries suffered while serving on active duty. How can there be no benefits for a child/family who participates in a research study? This needs to be changed to be fully approvable. **Compensation should be mandatory if there are complications which arise due to the procedures.**

3. "Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth in 45 CFR 46.408". As stated above, I feel there should be some changes made in the parental permission form. There needs to be **full compensation if there are complications that arise due to the procedures.** This is a major oversight and needs to be

corrected before the protocol is approved. Otherwise, the permission procedure is acceptable.

In closing, I feel that the protocol by Dr. Noah should be approved with the recommended changes. CF is a multifaceted disease and needs to be treated aggressively. Aggressive treatments are a direct result of aggressive research. I only hope that my child will benefit from this and future research studies.

Thank you for granting me the opportunity to represent the CF Children and their parents.

Sincerely,

Joan L. Hoopengardner
Mom of a Child with CF